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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,135	09/27/2001	Walter H. Gunzburg	2316.1002-001	2027

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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,135	GUNZBURG ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,8-17 and 22-25* is/are pending in the application.

4a) Of the above claim(s) *9-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,8 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/925214.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In the amendment filed December 13, 2004, applicant canceled claims 1-4, 18-21, amended claims 5, 8 and added new claims 23-25. Claims 5, 8-17 and 22-25 are pending, claims 9-17 are withdrawn from consideration due to a nonelected invention and claims 5, 8 and 22-25 are under consideration.

Request for Reconsideration

The request filed on 12/13/4 for a Request for Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/965135 is acceptable and a RCE has been established. An action on the RCE follows.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5, 8 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gunzburg et al. (Nature. 1993; 364 (July 8): 154-158), Gilboa (US 5,658,775) and Vile et al. (Cancer Research. 1993; 53 (5): 962-7, abstract only).

The claims are drawn to a retrovirus vector that is capable of undergoing promoter conversion and is replication defective. The retrovirus comprises, 5' to 3': U3-R-U5, a first coding sequence encoding a therapeutic peptide, a second sequence encoding a peptide with Sag activity that is linked to a promoter that is active in B and/or T cells and a 3'LTR comprising a

partially or completely deleted U3 region that comprises a tissue-specific promoter that regulates the expression of the first coding sequence, followed by R-U5.

The teachings of Gunzburg et al. and Gilboa are repeated herein. The difference between the claimed invention and the construct of Gunzburg et al. and Gilboa is the tissue specific promoter that replaces the 3' LTR and the B and/or T cell active promoter encoding Sag.

Vile et al. teach retroviral vectors expressing therapeutic genes with tissue specific promoters, see the abstract provided. One of ordinary skill in the art at the time the invention was made would have been motivated to express the heterologous therapeutic gene with a tissue specific promoter to express the gene of interest in a tissue of interest more specifically. One of ordinary skill in the art at the time the invention was made would also have been motivated to express Sag with a T and/or B cell specific promoter to optimize Sag expression in those cells for proliferation, taught by Gunzburg et al. One would also be further motivated to express Sag from a T and/or B cell specific promoter to regulate its expression separately from the therapeutic gene. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of expressing a tissue specific promoter in the 3' U3 region to regulate the expression of the first coding sequence because Gilboa teaches replacing the 3' U3 region with any heterologous promoter and heterologous sequence, see column 4, lines 27-32, column 4, line 56 to column 5, line 26, Figure 2C and claim 25.

Applicant argues that the vectors instantly claimed differ from Gilboa because they are not SIN vectors. Applicant states that the instant vectors regulate expression of a gene within the body of the vector after promoter conversion, which is completely different from the SIN vectors of Gilboa, in which the regulatory elements within the 3' LTR are inactivated.

A review of the references as well as applicant's arguments have been fully considered, but are found unpersuasive because there is no distinction found between the structural elements found in the 3' LTR instantly claimed and the 3' LTR of Gilboa. The instant construct requires that the U3 region of the 3' LTR to be completely or partially deleted and followed by R-U5. The construct of Gilboa also comprises a completely or partially deleted U3 region of the 3'LTR followed by R-U5, see claims 1, 4, 9, 10, 13, 15-17, 19-24 and Figures 4 and 10. Therefore, the structural features of the 3' LTR of the instant construct and the construct of Gilboa are indistinguishable. Applicant asserts that the only mechanism by which a SIN vector can express a gene within the body of the vector is if each gene is linked to a promoter within the body of the vector since the regulatory elements normally found within the 3' U3 sequence is inactivated. However, the instant construct claimed also has inactivated 3' U3 sequences since they are partially or completely deleted. The insertion of a functioning promoter (as applicant states would normally be present) at this defective site ensures expression of a heterologous gene upstream of the body of the vector once the virus is reverse transcribed. The replacement of the wild-type promoter for a promoter that is more specific to the heterologous gene insert would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to restore normal virus replication, control the amount of gene expression and ensure that the gene of interest is only expressed in specifically targeted sites, as evidenced by the teachings of Vile et al.

Applicant also asserts that the instant references do not suggest two coding sequences present within the body of the vector. However, claim 25 of Gilboa is specifically drawn to the retroviral vector "comprising a second, non-retroviral DNA sequence inserted between the 5'

LTR and the 3' LTR of the retroviral vector." The retroviral vector of Gilboa expresses a therapeutic protein, such as human adenosine deaminase (ADA) or a sequence from a pathogen or a hemoglobin protein, see column 8, line 66 to column 9, lines 1 and 13-29. The heterologous genes may be expressed from any promoter of interest, see column 4, lines 27-32, such as the tissue specific promoter taught by Vile et al. The construct of Gilboa also has Sag activity since Gunzburg et al. teach that Sag is present in the U3 region of the 5' MMTV LTR, see Figure 1a. The ordinary artisan would have been motivated to express Sag from a heterologous promoter to optimize Sag expression in T and/or B cells and to regulate its expression separately from the therapeutic gene.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-Th 6:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648